(d) contacting the amplified oligonucleotide with a fluorescent dye which binds to RNA directly and stains the oligonucleotide; and

(e) measuring fluorescence emitted from the stained oligonucleotide which is indicative of epitope detector bound to the surface and molecules expressing the selected epitope in the sample.

REMARKS

Claims 1-14 are pending in the instant application. Claims 2-14 have been withdrawn from consideration by the Examiner and subsequently canceled without prejudice by Applicants by this amendment. Claim 1 has been rejected. Claim 1 has been amended. No new matter is added by this amendment. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Finality of Restriction Requirement

The Examiner has made final the Restriction Requirement as set forth in the Office Communication mailed March 26, 2002. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have canceled non-elected claims 2-14, without prejudice. However. in light of the finality of this

Restriction Requirement, Applicants reserve the right to file a divisional application to the canceled subject matter.

II. Provisional Double Patenting Rejection under 35 U.S.C. § 101

Claim 1 has been provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claim 1 of copending Application No. 09/783,896.

Applicants respectfully traverse this rejection.

In accordance with MPEP § 804 and well established case law, a double patenting rejection under 35 U.S.C. §101 requires that identical subject matter be claimed. See e.g. Miller v. Eagle Mfg. Co. 151 U.S. 186 (1894); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Ockert, 245 F.2d 467, 114 USPQ 330 (CCPA 1957). Claim 1 of copending Application No. 09/783,896 is drawn to a method for detecting molecules expressing a selected epitope wherein in step (b) the surface is contacted with an epitope detector comprising an oligonucleotide attached to a monoclonal antibody for the selected epitope, a single chain Fv for the epitope or a constrained epitope specific CDR. In contrast, claim 1 of the instant application is drawn to a method for detecting molecules expressing a selected epitope wherein the epitope detector used in step (b) comprises an

oligonucleotide attached to a monoclonal antibody for the selected epitope, a single chain Fv for the epitope or a constrained epitope specific CDR, CDR mimetic or engineered CDR structure. Thus, these claims are not drawn to identical subject matter and rejection under 35 U.S.C. §101 is improper.

Withdrawal of this rejection under 35 U.S.C. § 101 is therefore respectfully requested.

III. Provisional Obviousness-type Double Patenting Rejection

Claim 1 has been provisionally rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11-14 of copending Application No. 09/783,896. The Examiner has acknowledged that the conflicting claims are not identical but suggests that they are overlapping in scope and not patentably distinct from each other.

As both applications are still in prosecution and may undergo further claim amendments which may render moot this provisional obviousness type double patenting rejection, it is respectfully requested that this rejection be held in abeyance until one of these applications has been allowed. At that time, should this obviousness-type double patenting issue still exist, Applicants will file the appropriate terminal disclaimer(s).

IV. Objection to the Specification

The Examiner has objected to the title as not descriptive of the invention to which the claims are directed. The Examiner suggests that the claim language is directed to a method of detecting molecules expressing a selected epitope via fluorescent dyes. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended the title to indicate the method which the Examiner suggests to be claimed. Specifically, the title has been amended to be "METHOD FOR DETECTING MOLECULES EXPRESSING A SELECTED EPITOPE VIA FLUORESCENT DYES". Withdrawal of this objection is respectfully requested in light of this amendment.

V. Information Disclosure Statement

The Examiner has indicated that references lined through in the copy of the Information Disclosure Statement provided with this Office Action were not considered because copies of the references were not provided with the application. It is respectfully pointed out, however, that copies of these references were already provided in prior pending U.S. patent applications which are clearly referenced on the Information Disclosure Statement filed in the instant application and which

are relied on in the instant application for an earlier effective filing date. The Information Disclosure Statements submitted in the earlier applications comply with paragraphs (a) through (c) of 37 C.F.R. 1.98. Thus, in accordance with 37 C.F.R. 1.98(d)(1) and (2), copies of patents, publications, pending U.S. applications or other information listed in this information disclosure statement which have been lined out by the Examiner were not required to be submitted in the instant application. Thus, consideration of these references by the Examiner is respectfully requested.

VI. Rejection of Claim 1 under 35 U.S.C. § 102(b)

Claim 1 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Suzuki et al. (Jpn. J. Cancer Res. 1995 Vol. 86, pg 885-889). Applicants respectfully traverse this rejection.

The Examiner suggests that Suzuki et al. discloses a sensitive method for the detection of antigen in sera in which a specific DNA molecule is used for a marker. According to the Examiner, Suzuki et al. teaches amplification by PCR of a biotinylated DNA complexed with antigen-antibody. Further, Suzuki et al. teaches staining of the amplified product with

ethidium bromide. Thus, the method of Suzuki et al. is used for DNA detection.

In contrast, in the instant invention RNA is being quantified and fluorescence dyes which stain RNA are used.

In an earnest effort to clarify this distinction, claim 1 has been amended to state that the amplified oligonucleotide is contacted with a fluorescent dye which binds to RNA directly. Support for this amendment can be found in the specification at page 14, lines 11-22 wherein it is taught that:

> [a] preferred means for detection in the present invention comprises staining with a fluorescent dye. In this embodiment, after RNA amplification with a polymerase such as T7 RNA polymerase, T3 RNA polymerase, SP6 RNA polymerase, φ29 polymerase or Taq polymerase, a portion of the reaction mixture can be mixed with a fluorescent dye such as RiboGreen reagent (Molecular Probes, Inc) (U.S. Patent 5,436,134), a unsymmetrical cyanine dye that binds to RNA directly in the solution and then releases fluorescence signals. Examples of other fluorescent dyes with similar properties useful in this method include, but are not limited to, PicoGreen, TOTO-1 or YOYO-1.

This teaching clearly supports amendment of claim 1 to include the limitation that the fluorescent dye binds to RNA directly Thus, no new matter is added by this amendment.

MPEP § 2131 is clear, to anticipate a claim the reference must teach every element of the claimed invention. Since Suzuki et al. do not teach or suggest use of fluorescent dyes which

bind to RNA in their DNA assay, this reference cannot anticipate the claims as amended.

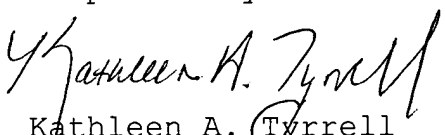
Withdrawal of this rejection under 35 U.S.C. § 102(b) is therefore respectfully requested.

VII. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,



Kathleen A. Tyrrell
Registration No. 38,350

Date: **November 5, 2002**

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please amend the specification as follows:

At page 1, lines 1-3, please insert the following title:

~~METHODS FOR IMMUNO-DETECTION OF EPITOPES ON MOLECULES AND FOR DETECTION OF INTERACTIONS OF MOLECULES VIA FLUORESCENT DYES~~

METHOD FOR DETECTING MOLECULES EXPRESSING A SELECTED EPITOPE VIA FLUORESCENT DYES

In the Claims:

Please cancel claims 2-14, without prejudice.

Please amend claim 1 as follows:

1. (amended) A method for detecting molecules expressing a selected epitope in a sample comprising:

(a) immobilizing a molecule expressing a selected epitope in a sample to a selected surface;

(b) contacting the surface with an epitope detector so that the epitope detector binds to immobilized molecules on the surface, said epitope detector comprising an oligonucleotide attached to a monoclonal antibody for the selected epitope, a single chain Fv for the epitope or a constrained epitope specific

CDR, CDR mimetic or engineered CDR structure;

(c) amplifying the oligonucleotide of said epitope detector;

(d) contacting the amplified oligonucleotide with a fluorescent dye which binds to RNA directly and stains the oligonucleotide; and

(e) measuring fluorescence emitted from the stained oligonucleotide which is indicative of epitope detector bound to the surface and molecules expressing the selected epitope in the sample.